**Structural Basis for Allosteric Activation of Ubiquitylation Mediated by Ube2g2 and gp78 RING Finger**

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Ube2g2 is an E2 ubiquitin-conjugating enzyme and gp78 is an endoplasmic reticulum-associated E3 ubiquitin ligase with the RING finger. Distinct from the RING finger, gp78 recruits Ube2g2 with its G2BR domain. The Ube2g2-G2BR interaction is specific with high affinity, induces significant conformational changes near the active site of Ube2g2, causes a 50-fold increase in the affinity between Ube2g2 and the RING finger, and results in markedly increased ubiquitylation by Ube2g2 and the gp78 RING finger (Molecular Cell 34, 674-685, 2009). Here, we report the crystal structure of the ternary Ube2g2-G2BR-RING complex at 2.3 Å resolution. The crystal belongs to space group \( P4_2_2_2 \), with unit cell parameters \( a = b = 58.25 \) and \( c = 158.43 \) Å. The structure shows that the G2BR and RING finger of gp78 bind to the opposite sides of the Ube2g2 molecule. Comparative analysis of the ligand-free Ube2g2 (PDB entry 2CYX), Ube2g2-G2BR (3H8K), and Ube2g2-G2BR-RING (this work) structures reveals structural basis for the allosteric activation of ubiquitylation mediated by Ube2g2 and the gp78 RING finger. The Ube2g2-G2BR-RING structure presented here is the first of its kind, shedding lights on the mechanism of other E3 ubiquitin ligases with the RING finger.

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